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Am 52 AH

Cap 2 A.H.D. No. 145

June 1952

UNITED STATES DEPARTMENT OF AGRICULTURE
Agricultural Research Administration
Bureau of Animal Industry

THE USE OF VITAMIN B₁₂ AND ANTI-BIOTIC SUPPLEMENTS
IN LIVESTOCK FEEDING

Animal protein feeds contain a number of factors, such as vitamins and minerals, necessary for the growth and reproduction of animals, in addition to the protein itself. As the knowledge of nutrition developed, certain nutritional properties, suggestive of unknown vitamins, were found to be closely associated with animal proteins. This unknown complex was termed the "Animal Protein Factor" (APF) until in 1948 when one of its constituents, vitamin B₁₂, was identified. While there are indications that other as yet unknown factors may be associated with vitamin B₁₂, the term "Animal Protein Factor" or "APF" has now been generally discarded in favor of "Vitamin B₁₂".

These nutrients must be present in a nutritionally adequate ration. Animals obtain these nutrients from their feed or by formation by micro-organisms in the digestive tract. The action of the microorganisms is especially important in cattle and sheep. Various byproducts of the meat packing and fishing industries are rich in vitamin B₁₂ and certain nutrients.

While animal products will continue to be the preferred source of certain nutrients necessary for animal production, the knowledge of their unique contribution to animal life has stimulated the search for such nutrients in plant feeds and animal byproducts, and the attempt to produce them with microorganisms. In this way, more of the desirable animal products become available for the use of man.

The need for additions of nutrients associated with animal feed varies with the kind of animal. Some of the nutrients are produced in gastro-intestinal tracts. This is especially true of the ruminant. Poultry and swine, with a simpler gastro-intestinal tract, do not have as active a microbiological action, hence it is necessary to provide more of the nutrients in the feed.

Among the more commonly used animal feeds containing vitamin B₁₂ are meat scraps, tankage, fish meal, condensed fish solubles, and similar products. Other important sources of vitamin B₁₂, however, from micro-organisms are now available. These consist of byproducts obtained from various industrial fermentation processes, including those obtained in the manufacture of the various antibiotics. Vitamin B₁₂ has not been found in plant feeds, at least in any considerable amount.

The primary importance of vitamin B₁₂, from whatever source derived, lies in its value as a supplement to all-vegetable diets or to diets low in animal protein. It should be noted, however, that the proteins of an all-vegetable diet are apt to be less satisfactory than animal proteins in respect to the proportions of the various amino acids entering into their composition. Even though supplemented with vitamin B₁₂, the vegetable proteins are, therefore, generally less efficient. When animal byproducts are replaced by plant source concentrates, attention should, therefore, be given to securing the best possible balance of the essential amino acids. When this is done and the necessary nutrients provided, plant proteins may be used successfully in animal production.

Much of the experimental work on vitamin B₁₂ has centered around diets based on combinations of corn and soybean meal. Additions of vitamin B₁₂ have resulted in decided improvements in feeding value, bringing the growth response in both pigs and chickens into line with those obtained when animal protein supplements are included in the diets.

Vitamin B₁₂ requirements of various animals have not been fully established as yet. However, the following may serve as a guide for feed formulation:

Poultry - Growing and breeding rations, 7-10 milligrams per ton of feed.

Swine - Growing and fattening, 10-18 milligrams per ton of feed.

Antibiotics

The nutritional spotlight, however, is now focused more particularly on the use of antibiotics in the feeding of farm animals. For the purpose of this discussion, antibiotics may be considered as organic compounds with germ-killing properties that are being used in the medical world for combating disease. Their growth stimulating value in animal feeding was recognized quite by accident. While searching for cheaper sources of vitamin B₁₂, investigators discovered that the microorganisms used in the production of certain antibiotics also produced substantial quantities of this vitamin during their growth. The residues remaining after the antibiotics had been removed was in a very short time offered to the feed industry for use as supplements to poultry and swine feeds. Investigators studying these products soon realized that they contained a substance or substances that gave growth stimulation over and above that which could be attributed to vitamin B₁₂. In 1950 it was reported by one group of workers that the substance responsible for the extra stimulation noted in their experiments must be aureomycin, the antibiotic from which their byproduct had been separated. It was further reported that the addition of pure aureomycin to chick starting rations resulted in a remarkable increase in growth rate. Shortly thereafter, numerous reports on the use of various antibiotics in poultry and swine feeding appeared.

Reports to date show that in many cases the antibiotics, streptomycin, aureomycin, bacitracin, terramycin, and penicillin are active in stimulating the growth of swine and poultry. These antibiotics are not always interchangeable on an equal weight basis so far as results are concerned. That is to say, it may take up to ten times as much of one antibiotic as it does of another to produce the same growth response under a particular set of conditions. In some cases, one antibiotic may be quite ineffective while another shows high growth stimulating activity. This may possibly be due to the general type of diet being used, to the condition of the animals at the time of supplementation, or to the presence or absence of specific disease producing organisms.

For example, the following levels in grams per ton of feed may be used as a guide for feeding antibiotics:

	Growing swine	Growing chickens
Aureomycin	10-20	7-10
Bacitracin	10-20	7-10
Penicillin	3-8	2-3
Streptomycin	15-30	20-40
Terramycin	10-20	7-10

The exact way in which these antibiotics function in causing growth stimulation is not clear at this time, although a number of hypotheses have been advanced. (1) Since these antibiotics possess germ-killing properties, they seemingly could help to control some of the infectious diseases of swine, particularly those affecting the digestive tract. This has been demonstrated by the control of some forms of scours and gastroenteritis. (2) The antibiotics might function in reducing the number of the types of intestinal bacteria that produce toxic products or that compete with the animal for certain vitamins and other nutrients in the diet. (3) Antibiotics, by their control of unfavorable bacteria, may permit the free growth of other bacteria that synthesize known or unknown growth factors in greater quantity. (4) Antibiotics, in killing intestinal micro-organisms, may make available to the animal various accessory substances otherwise retained within the bacterial cell. (5) Antibiotics may reduce the moisture content of the intestinal material, which then passes along more slowly, thus permitting more efficient utilization, or there may be a surface tension effect on the intestinal walls permitting better absorption of digested material. (6) Antibiotics might possibly have hormone properties. There is little direct experimental evidence, however, to support any of these hypotheses; nor has it been conclusively demonstrated that the antibiotics have a direct effect upon metabolism.

The "disease level" hypothesis has been advanced, also, to account for the variation in response to the various antibiotics on the same or different diets. The term "disease level" is defined as the degree of feed lot infestation with virus or bacteria which cause scouring in pigs. It is

suggested that the value of antibiotics in swine rations may depend upon the exposure to disease, increased responses being obtained as the incidence of disease increases. An experiment has been cited where a number of healthy, well fed pigs purchased from a disease-free farm and fed different levels of aureomycin failed to show any response to the antibiotic, apparently because of a low "disease level" or infestation with organisms causing diseases.

Also, in an experiment conducted at the Agricultural Research Center at Beltsville, certain groups of runts and unthrifty pigs that had been receiving a good quality of feed showed a surprising increase in growth rate in response to antibiotic supplementation. This would seem to indicate the existence of a bacterial infection and its control.

Composition of Experimental Diets Fed to the Three
Lots of Pigs

Ingredients	Lot 1 ^{1/}	Lot 2	Lot 3
	Percent	Percent	Percent
Ground yellow corn	70.0	69.7	69.7
Tankage (60% protein)	3.0	3.0	3.0
Fish meal	3.0	3.0	3.0
Soybean meal	10.5	10.5	10.5
Linseed meal	6.0	6.0	6.0
Alfalfa meal	6.0	6.0	6.0
Mineral mixture ^{2/}	1.5	1.5	1.5
Vitamin B ₁₂ concentrate ^{3/}	...	0.3	...
APP supplement ^{4/}	0.3

^{1/} Contained 18% crude protein, Assay indicated the presence of 6.7 mcg. of vitamin B₁₂ per pound.

^{2/} Mineral mixture was composed of:

Ground limestone 57.7 percent
Steamed bonemeal 20.0 " "
Iodized salt 20.0 "
Ferrous sulfate 2.0 "
Copper sulfate 0.1 "
Manganese sulfate 0.2 "

^{3/} Contained 3.5 mg. vitamin B₁₂ per pound.

^{4/} Contained 1.0 mg. vitamin B₁₂ and 0.6 gm. aureomycin per pound

On the nutritional side of the picture, another Beltsville experiment may be cited. Pigs receiving a diet deficient in niacin but adequate in other respects responded for a limited time to additions of pure aureomycin by growing at a rate equal to that of control pigs receiving niacin supplements. After the third week, however, the aureomycin was not effective in preventing deficiency symptoms. Where niacin was supplied with this diet, the further addition of aureomycin was without advantage.

Studies on the use of antibiotics in swine feeding are now being directed along the following lines:

- (1) Types of antibiotics that stimulate growth.
- (2) Relative value of the different antibiotics.
- (3) Mode of action in stimulating growth.
- (4) Effect on runts and unthrifty pigs.
- (5) Effect on the prevention and cure of disease.
- (6) Possibility of the development of resistant strains of pathogenic microorganisms.
- (7) Recommendations for practical usage.
- (8) Effect on breeding animals and their reproduction, performance, and the livability of the pig.
- (9) Effect on feed efficiency.
- (10) Effect of accelerated growth on carcass quality and presence of antibiotics in meat.

Under controlled laboratory conditions, growth responses to antibiotics ranging from 10 to 20 percent increase in case of the healthy pig, and up to 100 percent or more in case of runts or unthrifty pigs, have been reported. Farmers with somewhat less controlled conditions are reporting excellent results not only with growing-fattening hogs but also with breeding stock where larger and more uniform litters are being weaned. Research institutions as well as the companies manufacturing these products are encouraging the testing of antibiotics under all farm and feed lot conditions better to evaluate the feeding possibilities.

The effects of antibiotics on feed efficiency or efficiency of feed utilization from the standpoint of pounds of feed per 100 pounds gain in body weight have not been completely evaluated. In some cases results have been reported of the need for less feed to bring hogs to market weight, while in other cases no reduction in feed requirement was noted. In any event, no cases have been reported where the reverse was true. One over-all advantage in adding antibiotics is that if stimulation of growth occurs, the animals will be ready for market at a much earlier date, thus often commanding a better market price.

The question might be asked as to what effect the antibiotics have on the carcass value from the standpoint of fatness versus leanness and also from the standpoint of the amounts of residual antibiotic remaining in the meat offered to the consumer. Very little information is now available on the amount of fat laid down during the increased growth rate; but information should be forthcoming very soon from experiment stations and from meat packing houses which will offer some clue as to effect on carcass value.

The question as to whether antibiotics can be fed in amounts high enough to be dangerous or toxic does not appear to be serious. The recommended levels for feeding are much lower than those used in the treatment of swine diseases. Also, existing feed control regulations state that

"the label shall bear the legend 'For Feeding Use Only'. Directions for use shall provide for incorporating not more than 50 grams of antibiotic per ton of finished feed."

There has been some question as to the possibility that the feeding of antibiotics might lead to the development of resistant strains of disease producing bacteria. Evidence on this point is lacking. Yet assuming that resistant strains should develop, it is possible that the mere shifting to another antibiotic or combination of antibiotics could be expected to eliminate this difficulty.

One of the latest proposals in swine feeding is that of removing new-born pigs from the sow immediately and rearing them on artificial milk, thus enabling the sow to produce three litters per year. Successful rearing of baby pigs by this method has in fact been reported, and substitute milks are being prepared by several firms. These products are designed to compare with sows' milk in feeding value. Since, however, they may be used under conditions where the pigs lack the antibodies against disease, they have been formulated to contain antibiotics to help guard against disease as well as to stimulate growth. To what extent the suggested innovation may prove practical remains to be seen.

Most of the information on the response of swine to antibiotics has come from the laboratories of universities, experiment stations and other research institutions. However, the antibiotic development has moved from the laboratory to the farm with surprising rapidity. In recent months, more and more information is coming from the farm where the ultimate decision will be made as to the economic value of antibiotic feeds.

Recommendations for practical farm usage are somewhat limited. Investigations at various State experiment stations have demonstrated that the type of diet and the effect on the intestinal flora will have a lot to do with the beneficial effects to be obtained with the various antibiotic supplements. It seems that the only sure way to be certain of the effect of an antibiotic or combination of antibiotics is to test them with the type of ration being used. The growth response to be expected may vary widely with the kind and amount of antibiotic used, the kind and condition of the animals, the sanitary conditions existing, and possibly other factors.

In any event, it should be pointed out that even though antibiotics may help to cure or prevent disease, they should not be used as substitutes for good sanitary feeding practices. It should also be pointed out that antibiotics cannot overcome nutritional deficiencies in a feed. That is to say, they will not take the place of other nutrients such as vitamins and amino acids or minerals that may be lacking in the feed. Thus antibiotic supplements do not make a wonder feed out of a poor or inferior feed but under suitable conditions permit the more efficient utilization of a good quality feed.

Until recently, antibiotic-containing products were designated as APF (animal protein factor) concentrates with no indication of their potency. In October, 1950, the Association of American Feed Control Officials formulated tentative definitions to distinguish between vitamin B₁₂ and antibiotic activity. These definitions are as follows:

"Vitamin B₁₂ Supplement is a feeding material used for its vitamin B₁₂ activity. It shall contain a minimum vitamin B₁₂ activity of 1.5 milligrams per pound. The term shall not be applied to products for which there are accepted names and definitions."

"Antibiotic Feed Supplement is a feeding material used for its antibiotic activity. It shall contain a single antibiotic or combination of antibiotics having growth-promoting properties. The name and amount of each antibiotic shall be declared on the label. It shall contain a minimum of 1 gram per pound of antibiotics."

A number of drug manufacturers are now marketing antibiotic supplements for use in swine and poultry feeds. Furthermore, these antibiotic supplements are widely used in commercial mixed feeds. Following is a list of companies which manufacture and sell concentrates containing vitamin B₁₂, antibiotics or both:

Commercial Solvents Corporation
Agriculture Division
Terre Haute, Indiana

Lederle Laboratories Division
American Cyanamid Company
Pearl River, New York

Merck and Company, Inc.
Rahway, New Jersey

Chas. Pfizer and Company, Inc.
630 Flushing Avenue
Brooklyn 6, New York

U. S. Industrial Chemicals, Inc.
60 East Forty-Second Street
New York 17, New York

These companies are listed for your information only and bear no endorsement by the Department. No discrimination is intended in listing these and omitting the names of other companies.

The use of antibiotics in animal feeding has raised many questions, both from the standpoint of value and also possible ill effects. We should keep in mind that although the effects of long-time feeding of antibiotics have not been determined they seem for the present to have acquired an important place in the nutrition and feeding of farm animals.

